CLAIMS:

1. A tracer suitable to be used as a label of a molecule or material involved in chemical or biological reactions, the tracer comprising an particle that can be imaged as having a specific distinguishable shape, the shape used as particle identifier.

2. The tracer of claim 1, wherein the shape is a two-dimensional shape.

3. The tracer of claim 2, wherein the particle includes at least a notch as an orientation mark.

4. The tracer of any one of claims 1 to 3, wherein the particle is made of silicon.

5. Process for the manufacture of a tracer according to any one of claims 1 to 4, comprising shaping a suitable material into a specific distinct shape.

6. The process of claim 5, wherein the particle has a two-dimensional shape, the process comprising:

outlining a desired shape in a layer of a suitable material, obtaining a shape outline in the material; and

etching or impressing the shape outline into the material.

7. An assembly suitable for use as a label of a molecule or material involved in a reaction, the assembly comprising a tracer, the tracer comprising a particle having specific distinct shape according to any one of claims 1 to 4, and a readable support associated with the particle to render the shape of the particle identifiable.

8. The assembly of claim 7, wherein the readable support is a two-dimensional support.

9. The assembly of claim 8, wherein the support is a microscope slide.

10. The assembly of claim 8 or 9, wherein the support is a patterned or sticky surface.

11. The assembly of any one of claims 8 to 10, wherein the support is at the bottom of each well in well-plate.

12. Process for manufacturing an assembly according to any of claims 7 to 11, comprising assembling a tracer according to any of claims 1 to 4 with a readable support suitable to be used to identify the tracer.

13. The process of claim 12, further comprising aiding positioning of the tracer on the support.

14. The process of claim 13 wherein aiding position of the tracer is performed by mechanical agitation or vibration.

15. Method to trace a molecule in a chemical or biological reaction comprising coupling the molecule or material with the tracer of any one of claims 1 to 4, or the assembly of any one of claims 7 to 11.

16. The method of claim 15, wherein the molecule is DNA, RNA, or a protein, or the material is a cell or cell membrane.

17. The method of claim 16, wherein the molecule is DNA and the assay is DNA hybridization.

18. Method to perform a reaction wherein one or more molecules (or materials) are to be labeled, comprising:

coupling each of the one or more molecules with a tracer according to any one of claims 1 to 4, or with the assembly of any of claims 7 to 11, each tracer or assembly coupled with the each of the one or more molecules uniquely labeling the each of the one or more molecules.

19. The method of claim 18, further comprising:

reading the shape of the tracer coupled with the each of the one or more molecules, thereby identifying the molecule.

20. The method of claim 18 or 19, wherein the reaction is carried out to perform an assay and the molecule (or material) is a biological or chemical probe to be used in the assay

21. The method of claim 18 or 19, wherein the molecule is the sample to be assayed.

22. The method of claim 10, wherein the assay is a microarray assay.

23. The method of any one of claims 18 to 22, wherein the molecule is DNA, RNA, or a protein.

24. The method of claim 23, wherein the molecule is a DNA probe and the assay is a gene expression assay or polymorphism detection assay.

25. The method of claim 20 and 22 to 24 when depending on claim 20, wherein the probe is an oligonucleotide and coupling of the oligonucleotide with the tracer is performed by synthesizing the oligonucleotide on the tracer.

26. A method to perform an assay wherein a probe is reacted with a test sample, the method comprising:

coupling the tracer of any one of claims 1 to 4 with the probe or the test sample;

reacting the probe with the test sample;

assembling the tracer with a readable support allowing identification of the tracer; and

reading the support, thereby identifying the tracer.

27. The method of claim 16, wherein reacting the probe with the test sample is performed after coupling the tracer with the probe and before assembling the tracer with a readable support.

28. The method of claim 26 or 27, wherein assembling the tracer with the readable support is performed after coupling the probe with the tracer and but before reacting the probe with the test sample.

29. The method of any one of claims 26 to 28, wherein reading the support thereby identifying the tracer is performed by taking micrographic images of the support.

30. The method of any one of claims 26 to 30, wherein the assay is a microarray assay.

31. The method of any one of claims 26 to 30, wherein the probe is DNA probe and the assay is a gene expression assay or polymorphism detection assay.

32. A method to perform an assay wherein a probe is reacted with a test sample, the method comprising:

coupling the probe or the test sample with the assembly comprising a tracer and a readable support making the tracer identifiable according to any one of claims 7 to 11;

reacting the probe with the test sample; and

reading the support, thereby identifying the tracer.

33. The method of claim 32, wherein reacting the probe with the test sample is performed after coupling the tracer with the probe or test sample.

34. The method of claims 32 or 33, wherein the assay is a microarray assay.

35. The method of any one of claims 32 to 34, wherein the probe is DNA probe and the assay is a gene expression assay or polymorphism detection assay.

36. Kit of parts to label a molecule involved in a chemical or biological reaction, the kit comprising:

a tracer according to any one of claims 1 to 4, the tracer comprising a particle having a specific distinct shape, the shape used as particle identifier; and

a readable support associated with the particle to make the shape of the particle identifiable,

the tracer and the readable support to be used in the method according to any one of claims 18 to 25.

The kit of parts according to claim 36, wherein

37. The tracer and the support are included separately and/or in an assembly according to any one of claims 7 to 11.

38. A process for generating novel enhanced shape encoding particles (SEP's) which maximizes particle encoding capacity and reserves a centralized probe attachment zone, comprising the steps of:

fabricating a planar poly-layered silicone wafer flake further comprised of a first micron-scale thickness polycrystalline Si layer disposed upon a bottom thinner dissolvable layer of SiO_2;

photolithographically etching with reactive ions desired geometric shape outlines in the top Si layer;

releasing resulting shaped flakes by dissolving the bottom dissolvable layer of SiO_2 with HF acid whereby said desired geometric shape outlines further comprise peripheral notches extending not more than 1/6 th of the diameter of the resulting shaped flakes into a central region of the resulting shaped flakes.

40. A product produced by the process of claim 38.

41. In a process for encoding the identity of microscopic particles by shape, wherein such particles can be combined in large numbers while remaining readily distinguishable and having their individual identities recovered, the improvement comprising:

fabricating a multiplicity of shape encoded particles (SEP's) each having a top surface and a bottom surface and each having a unique geometric configuration wherein each of said multiplicity of SEP's is effective for being readily arranged such that each of the top and bottom surfaces rests in a plane parallel to a plane of a surface upon which the bottom surface is disposed enabling display of a definitive outline when imaged by a suitable technique.

42. A novel enhanced SEP product, produced by the process of claim 41, wherein a definitive outline enables identification of the SEP and any material previously associated with the SEP through at least one of binding and contact with the SEP.

43. A novel enhanced SEP product, produced by the process of claim 41, having a dimensional range extending from the nanometer to the millimeter scale.

44. A novel enhanced SEP product, produced by the process of claim 41, wherein shape detection is accomplished by at least one imaging technique selected from the group consisting of optical microscopic imaging, near field microscopy, electron microscopy, scanning-tunneling microscopy and atomic force microscopy.

45. A novel enhanced SEP product, produced by the process of claim 41, wherein resolution of the definitive outline of said SEP is facilitated by automated image recognition software.

46. A novel enhanced SEP product, produced by the process of claim 41, wherein the SEP has a diameter of less at least about three microns and said unique geometric configuration is less than the wavelength of visible light.

47. A novel enhanced SEP product, produced by the process of claim 41, effective to transport organic matter bound to the top surface of said SEP.

48. A novel enhanced SEP product, produced by the process of claim 41, effective to transport inorganic matter attached to the top surface of said SEP.

49. A novel enhanced SEP product, produced by the process of claim 41, wherein said SEP is effective for use in conjunction with numerous other novel enhanced SEP's for massive simultaneous tracking of material bound to the top surface of said SEP's as the SEP's are pooled and put through at least one of a simple reaction and a series of pooled reactions.

50. A method for generating shape encoded response classes for use in subsequent assays, comprising the steps of:

providing a multiplicity of novel enhanced SEP's;

attaching probes to each of the multiplicity of SEP's;

reacting the multiplicity of SEP's having bound probes against a sample;

physically sorting the resulting products into at least two classes using respective strengths of reporter signals; and,

decoding the results by automated shape imaging by class.

51. The method of claim 50, wherein the providing step further comprises: fabricating bulk quantities of SEP's.

52. The method of claim 11, wherein the attaching step further comprises undergoing an attachment reaction to form SEP-probe conjugates.

53. The method of claim 52, wherein the reacting step further comprises pooling the SEP-probe conjugates and dispensing randomly sampled aliquots.

54. The method of claim 53, wherein the sorting step further comprises performing individual assays.

55. The method of claim 54, wherein the decoding step further comprises using an automated imaging system.

56. The method according to claim 55, wherein the decoding step further comprises usingshape recognition software to generate a desired form and format for a resulting data set.

57. The method of claim 57, wherein massively multiplexing assays are accomplished using fewer spatial limitations and mixing constraints relative to existing methods of multiplexing probes.

58. The process of claim 41, wherein the fabricating step further comprises maintaining a special free region optimal for probe attachment and detection on the top surface of said SEP, further reducing a likelihood of artifactual debris masking the unique geograph features imaged.

59. A product, produced by the process of claim 58, which includes an addressable microreactor comprised of an encoded microwell.

60. The process of claim 41, further comprising one-bit SEP imaging.

61. In a generally planar shape encoded particle (SEP) made from a geometric base shape for arbitrarily large capacity and unambiguous multiplexed decoding, the improvement which comprises:

an adjustable coding capacity defined by a number of independent notches extending along a peripheral edge surface of the SEP whereby N notches encode for 2^N shapes.

62. The SEP of claim 61, wherein the systematic notch patterns are defined by a following algorithm ("notching equation"):

i. $S[C](t) = b_0(t) + c_1 b_1(t) + c_2 b_2(t) + \ldots + c_N b_N(t)$

ii. given a code word consisting of N digits in base k,
$C = (c_1, c_2, \ldots, c_N)$,

iii. where $c_i \in \{0,1,\ldots,k-1\}$ (e.g., k = 2 is binary code, each c_i is 0 or 1), it is associated with a 2-dimensional closed curve S[C]—the "shape"—defined by the "notching equation"

iv. where $t \in [0,1]$ is a parameterization of the base shape boundary curve. Here, $b_0(t)$ represents the equation of the base shape boundary, and the other $b_i(t)$ represent the equations of the basis of curves corresponding to the distinct potential "notches". The number of distinct code words, C, is k^N (2^N for binary coding).

63. The SEP of claim 62, further comprising being distinguishable in any orientation by having at least an indicum to differentiate the spatial orientation of the SEP in terms of the relative position of the SEP upon at least one of a substrate upon which it is disposed and a material in which it is embedded.

64. The SEP of claim 63, wherein the image of S[C] is the boundary of a connected open set, further defined as the SEP is capable of being repeat manufacturable in that if the shape was cut from a material sheet, the SEP is substantilaly free of dangling or disjoint parts interfering with the ability to distinguish the shape of the SEP.

65. The SEP of claim 64, wherein a perturbing basis $b_i(t)$ corresponds to isolated notches positioned about the peripheral edge of the geometric base shape.

66. The SEP of claim 65, wherein said base shape is a square; and the isolated notches further comprise completely disjoint smaller square notches.

67. The SEP of claim 64, wherein a perturbing basis bi(t) corresponds to distinct frequencies of sinusoidal ripples defined by distinct Fourier Modes along the boundary of a circular base geometric shape.

68. The SEP of claim 64, wherein a perturbing basis bi(t) corresponds to the first N nodes of a wavelet basis, defined by positional frequencies having specific mathematical properties for curves along the geometric base shape perimeter.

69. The SEP of claim 61, further comprising a multiresolution (fractal) curve defined by a following algorithm:

i. $S[C_{i+1}](t) = S[C_i](t) + c^i_1 b^i_1(t) + c^i_2 b^i_2(t) + \ldots + c^i_{Ni} b^i_{Ni}(t)$

ii. given any series of M base k code words of the type above, $X = \{C_1,\ldots,C_i,\ldots,C_M\}$, the single shape defined by this entire series, S[X], is defined iteratively as follows: the first iteration, $S[C_1]$, is defined as usual above, relative to some base shape;

iii. where $S[C_i]$ plays the role of the base shape for this step, and b^i_m is a basis of perturbations along this new base shape. These will typically be a reduced scale form of the type of notches used on the coarsest scale. The final or limiting shape produced by this process, $S[C_M]$, is the shape S[X]. The number of encoding shapes described this way is the number of encoding vectors, X, which is k^N, where N is now the total number of encoding digits in X, $N = N_1 + N_2 + \ldots + N_M$.

70. The SEP of claim 69, further comprising being distinguishable in any orientation by having at least an indicum to differentiate the spatial orientation of the SEP in terms of the relative position of the SEP upon at least one of a substrate upon which it is disposed and a material in which it is embedded.

71. The SEP of claim 70, wherein the image of S[C] is the boundary of a connected open set, further defined as the SEP is capable of being repeat manufacturable in that if the shape was cut from a material sheet, the SEP is substantially free of dangling or disjoint parts interfering with the ability to distinguish the shape of the SEP

72. The SEP of claim 64, further defined by a concise scalable and general specification language comprising a definitive size for the geometric base shape and a plurality of basis coefficients further describing the shape.

73. A process for designing a photolithography mask for high density fabrication of SEP's, comprising the steps of:

choosing a standard polygon which polygon surrounds a desired shape circumferentially;

replicating the standard polygon in a high density closed space regular array for defining available shape positions by covering the available mask area with N polygons; and

populating available locations on the mask given a set of N desired shapes.

74. The process of claim 73, implemented in software further comprising the steps of:

inputting a mask size, a standard polygon size and a specification history listing of desired N shapes;

translating the description into mask pattern specifications; and

automatically producing as output a mask specification file suitable for reading a pattern generator system used to fabricate the mask.

75. The process of claim 74, further comprising the steps of:

placing the N desired shapes on a mask for a single wafer;

etching the single wafer;

releasing the entire set of shapes; and

collecting the entire set of shapes into a single pool.

76. The process of claim 73, further comprising the steps of:

using the resulting mask to perform reactive-ion-etching of a silicon-on-insulator wafer; by,

reactive ion etching for sufficient time to cut through to the substrate;

subdividing the etched wafer into sub-sections for subsequent handling;

physically releasing the etched poly-crystalline silicon by dissolving the substrate with a hydrofluoric acid treatment;

creating a resulting pool of freed SEP's;

surface treating the freed particles with at least one of heating and hydrogen peroxide treatment to prepare the SEP's for subsequent handling; and,

storing the finished SEP's in purified H_20.

77. The SEP of claim 66, consisting essentially of a flake derived from a wafer of silicon.

78. The SEP of claim 66, consisting of a material selected from the group of

79. The SEP of claim 66, further comprising a magnetic material selected from the group consisting of magnetic, ferromagnetic and magnetizable components.

80. A method of using shape encoded particles (SEP's) for DNA analysis, which comprises the steps of:

providing a multiplicity of SEP's having distinct and imageable shapes;

binding each of said multiplicity of SEP's having distinct shapes to a desired number of biological probes;

hybridizing the resulting combinations in solution; and

acquiring data in the form of reporter signals from the bound material.

81. The method of claim 80, said providing step further comprising each of the multiplicity of SEP's having the inherent ability to both identify material bound to them and to track history of exposure as processing reaction steps alter their respective states or the state of organic probes bound to them.

82. The process of claim 38, said centralized probe attachment zone further comprising at least an encoded microwell having a diameter l ranging from at least about 1 micron to 100 microns and a volume less than or equal to 1

nano liter.

83. A product, produced by the process of claim 82.

84. A genomic analysis method, using the product of claim 82, comprising the steps of:

coupling biological probes to the novel enhanced SEP's having microwells;

mixing all of the novel enhanced SEP's having microwells together;

loading reaction mixutures into the microwells by soaking;

sealing the reaction wells;

and monitoring the reaction.

85. The method of claim 84, further comprising:

transferring the loaded particles from their aqueous loading solution into oil, forming a tension seal of the microwells;

transferring the aqueous loading solution and particles onto a soft polymer support surface, and impressing them into the surface with sufficient force based up the centrifuge acceleration to form a pressure seal of those microwells facing downward into the polymer;

transferring the aqueous loading solution and particles onto a support surface and impressing upon them a compliant polymer sheet with adequate force to form a pressure seal on those microwells facing upward into the sheet; and

undergoing a capping reaction whereby a multiplicity of spherical particles are introduced into the aqueous loading solution having a predetermined size and surface coating for fitting the multiplicity into the microwell openings and seal the microwell openings.

86. The method of claim of claim 85, further comprising Polymerase Chain Reaction (PCR) detection of DNA and RNA.

87. The method of claim 86, the PCR being used for DNA analysis whereby the shape encoded microwells are preloaded with PCR detection primers bound to the microwell walls having different shapes carrying different detection primers, and the pool of the microwell particles is introduced into the DNA sample to be analyzed, loaded by soaking and then sealed, reacted with PCR and imaged for a reporter signal to detect and quantify whether the subject DNA sample contains fragments corresponding to the involved detection primers.

88. The method of claim 87, further comprising using the reporter signal to for biodefense monitoring by simultaneously screening a sample for DNA from a multiplicity of pathogenic microorganisms and different strains of particularized pathogens.

89. The method of claim 85, further comprising Enzyme Linked Immunosorbant Assay (ELISA) detection of proteins.

90. The method of claim 89, whereby the shape encoded microwells are preloaded with ELISA detection antibodies bound to the microwell walls having different shapes containing different detection antibodies for different proteins, and The pool of the microwells is introduced into the protein sample to be analyzed In solution, loaded by soaking, and sealed, reacted and imaged for a reporter Signal to detect and quantify whether the sample contains proteins corresponding to subject detection antibodies.

91. The method of claim 90, further comprising using the reporter signal to for biodefense monitoring by simultaneously screening a sample for DNA from a multiplicity of pathogenic microorganisms and different strains of particularized pathogens.

92. The genomic analysis method of claim 85, the monitoring step further comprising using a fluorescent microscope or scanner to detect at least one of a positive signal (reaction) and a negative signal (no reaction).

93. A method of use of the SEP of claim 61, as an embedded identification device for bulk materials, whereby a multiplicity of said SEP's are at least one of surface coated onto workpieces; embedded into solid materials during manufacturing; mixed into powdered materials; and suspended in liquid or gas phase materials.

94. A method of use of the SEP of claim 62, as an embedded identification device for bulk materials, whereby a multiplicity of said SEP's are at least one of surface coated onto workpieces; embedded into solid materials during manufacturing; mixed into powdered materials; and suspended in liquid or gas phase materials.

95. A method of use of the SEP of claim 61, as an embedded identification device for military, police, criminal or terrorist activities by rendering specialty plastic, ceramic and metallic items traceable to their owners, manufacturers, or distributors.

96. The method of claim 95, further comprising emplacing SEP's within explosive devices.

97. A method of use of the SEP of claim 61, as an embedded identification device for high value components subject to theft.

98. A method of use of the SEP of claim 61, as an embedded identification device for sample tracking in forensic or biomedical analyses.

99. A method of use of the SEP of claim 61, as an embedded identification device for quality control in mixture based procedures.

100. A method of use of the SEP of claim 61, as an embedded identification

device for materials released into the environment.

101. A method of use of the SEP of claim 61, as an embedded identification device for rapid screening of different trial mixtures having a desirable property or ingredient.

102. A method of use of novel enhanced SEP's comprising the steps of:

generating a library of possible combinations of an identifiable set of molecular building blocks;

testing the molecular building blocks for a set of desired properties;

storing results on a number of N SEP's.

103. The method of claim 102, further comprising providing a stem cell line, cultured onto the N shape encoded particles a tracking assay from the to screen a large number of treatment series corresponding to exposure to or withdrawal of different growth factors and measuring by a reporter for a particular cell type.

104. A shape encoded particle (SEP) based combinatorial synthesis process, comprising the steps of:

providing a mutliplicity of novel enchanced SEP's which are effective for two-dimensional image creation over a massive number of possible combinations of geometric shapes by enabling display of a definitive outline when imaged by a suitable technique;

synthesizing directly onto the SEP's a predetermined range of combinations of chemical moieties and entities to be systematically tested for functionality;

whereby an encoded screening assay is created of the directly synthesized combinations of chemical moieties and entities such that a library of the same is created.

105. The process of claim 104, wherein an SEP combinatorial treatment tracking assay is generated by a series of steps, comprising, in combination:

starting with a series of cells;

tracking the response of the cells to a predetermined series of possible sequential treatments by a set of factors, wherein the order of application is important;

archiving the resulting data by SEP information; and

repeating the process X times as needed.

106. The process of claim 105, the tracking step further comprising:

carrying out a predetermined universe of possible combinations of treatment on a material;

recording the outcome of the possible treatment series;

divding a particle pool of resulting outcomes onto N distinct SEP shapes;

pooling the resulting SEP's;

arbitrarily dividing the SEP's into a plurality of treatment sub-groupings;

imaging the sub-groupings in such a way that the outcome is accociated with the shapew of each particle.

107. The process of claim 106, the carryinjg out step further comprising:

providing a set of chemical building blocks;

linking the building blocks to form a k-mer, or string of K linked blocks;

preparing a pool of N distinct SEP shapes;

undertaking a derivatizing reaction on the pool to prepare the SEP particles surfaces;

dividing the SEP pool randomly into M equal sub-pools;

iamging eahc sub-pools to record which shapes are included; and

repeating the process for K times.

108. A product produced by the process of claim 107 which is a shape encoded library.

109. The process of claim 105, the an SEP combinatorial treatment tracking assay is effective for producing a library of serially treated materials or an assay for a treatment series producing a design effect on the starting material.

110. A method of use of novel enhanced shape encoded particles (SEP's) for structural geometric forensic reconstruction comprising the steps of:

creating a pool of N distinct SEP's, from a single etching process;

applying the SEP's to the surface of a completed structure;

imaging the entire structure in a series of shape recording images mapped in three ordinal planes onto the structure; and,

retracing the structure from a fragment following a partially destructive event.

111. A method of use novel enhanced SEP's for seeding cultured pearls, comprising the steps of:

emplacing an SEP as a seed particles with a pearl culturing medium in the place of a standard seeding particle such as an oyster shell spherule;

recording the encoded identity of the SEP; and,

imaging the SEP non-destructively with x rays;

for at least one of authentication, tracing, theft prevention and reclamation.